I. AMENDMENTS

Amendments to the Claims:

This listing of claims will replace all prior versions, and listings, of claims in the application:

Listing of Claims:

The following Listing of the Claims replaces all prior versions, listings and amendments.

Claims 1. to 16. (Canceled).

17. (Previously Presented) The method of claim 26, further comprising contacting the cell with an effective amount of a compound that diminishes intracellular thymidine or purine, wherein said compound is 6-mercaptopurine, thioguanine, or 2'-deoxycoformycin.

18. (Canceled).

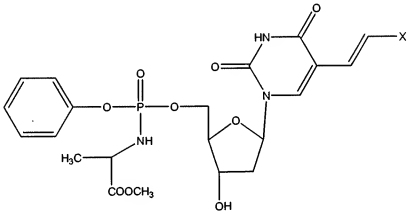
19. (Canceled).

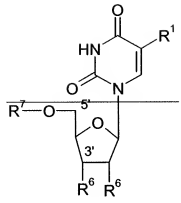
20. (Currently Amended) A method for screening for therapeutic agents for administration in combination with (E)-5-(2-bromovinyl)-2'-deoxy-5'-uridyl phenyl L-alaninylphosphoramidate or (E)-5-(2-bromovinyl)-2'-deoxy-5'-uridyl phenyl L-alaninyl monophosphate, comprising contacting the candidate therapeutic agent and (E)-5-(2-bromovinyl)-2'-deoxy-5'-uridyl phenyl L-alaninylphosphoramidate or (E)-5-(2-bromovinyl)-2'-deoxy-5'-uridyl phenyl monophosphate with a cancer cell selected from the group consisting of a breast cancer cell, a non-small cell lung cancer cell, a rectal cancer cell, a head and neck cancer cell, a stomach cancer cell, a pancreatic cancer cell, a colon cancer cell, a liver cancer cell, a gastric cancer cell, a skin cancer cell, a bone cancer cell, a bone marrow cancer cell, a testicular cancer cell, a brain cancer cell, a lung cancer cell, a prostate cancer cell and an ovarian cancer cell, and wherein said ~~hyperproliferative~~ cell ~~that overexpresses endogenous~~ endogenously overexpresses, intracellular thymidylate synthase enzyme and assaying for cell death.

21. (Previously Presented) The method of claim 20, further comprising contacting a normal cell with the candidate therapeutic agent and (E)-5-(2-bromovinyl)-2'-deoxy-5'-uridyl phenyl L-alaninylphosphoramidate or (E)-5-(2-bromovinyl)-2'-deoxy-5'-uridyl phenyl monophosphate and assaying for cell death.

Claims 22. to 25. (Canceled).

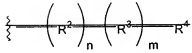
26. (Currently Amended) A method for inhibiting the proliferation of a cancer cell selected from the group consisting of a skin cancer cell, a bone cancer cell, a bone marrow cancer cell, a testicular cancer cell, a brain cancer cell, a lung cancer cell, a prostate cancer cell and an ovarian cancer cell, and wherein said cell that endogenously overexpresses thymidylate synthase ~~and wherein the cancer cell is selected from the group consisting of skin, bone, bone marrow, testis, brain, liver, lung, prostate and ovary,~~ the method comprising contacting the cell with an effective amount of a compound having the structure:





~~wherein:~~

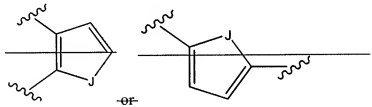
~~R^1 is of the formula:~~



~~wherein R^2 is one of:~~

~~an unsaturated C2 to C4 hydrocarbyl group;~~

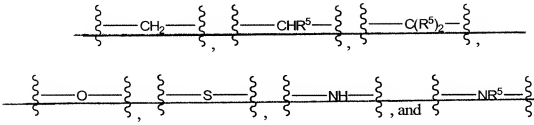
~~a heteroaromatic group having the structure:~~



~~or~~

~~wherein J is O, S, Se, NH, or NRALK, wherein RALK is a linear or branched alkyl having 1 to 10 carbon atoms or a cycloalkyl group having 3 to 10 carbon atoms;~~

~~R^3 is selected from the group consisting of:~~

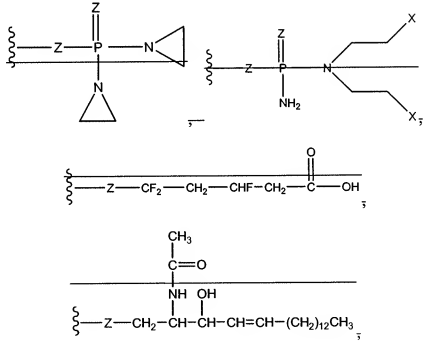


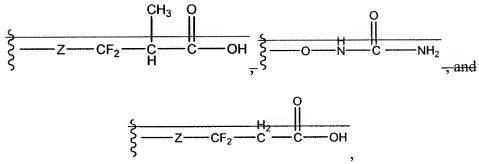
~~wherein R^5 may be the same or different and is independently a linear or branched alkyl group having from 1 to 10 carbon atoms, or a cycloalkyl group having from 3 to 10 carbon atoms;~~

~~wherein n is an integer from 1 to 10;~~

~~wherein m is 0 or 1;~~

~~wherein R^4 is a toxophore selected from the group consisting of:~~





wherein X is -Cl, ~~-Br,~~ or -I, ~~or other halogen, with the proviso that when R^7 is -H, and m is zero, then R^4 is not a halogen or when m is zero and n is zero, then R^4 is not a halogen;~~

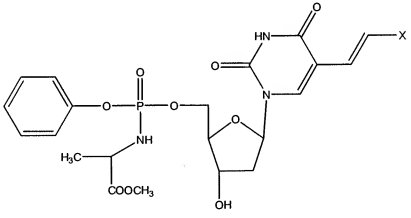
~~wherein Z is independently O or S;~~

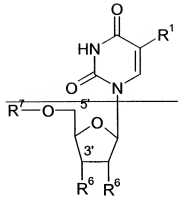
~~wherein R^7 is hydrogen, a monophosphate or a phosphoramidatyl derivative of an amino acid;~~

and wherein said compound may be in any enantiomeric, diasteriomeric, or stereoisomeric form, consisting of a D-form, L-form, α-anomeric form, and β-anomeric form.

Claims 27 and 28. (Canceled).

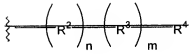
29. (Currently Amended) A method for inhibiting the proliferation of a cancer cell selected from the group consisting of a breast cancer cell, a non-small cell lung cancer cell, a rectal cancer cell, a head and neck cancer cell, a stomach cancer cell, a pancreatic cancer cell, a colon cancer cell, a liver cancer cell, a gastric cancer cell a skin cancer cell, a bone cancer cell, a bone marrow cancer cell, a testicular cancer cell, a brain cancer cell, an ovarian cancer cell, a lung cancer cell, a prostate cancer cell and an ovarian cancer cell, and wherein said cell ~~that~~ endogenously overexpresses thymidylate synthase, the method comprising contacting the cell with an effective amount of 5-Fluorouracil or Tomudex ~~a compound that inhibits thymidylate synthase activity~~, subsequent to contacting the cell with an effective amount of a compound having the structure:





~~wherein:~~

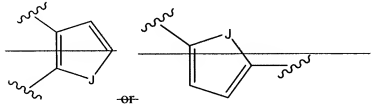
~~R^1 is of the formula:~~



~~wherein R^2 is one of:~~

~~an unsaturated C2 to C4 hydrocarbyl group;~~

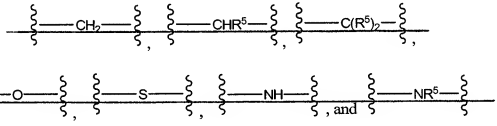
~~a heteroaromatic group having the structure:~~



~~or~~

~~wherein J is –O–, –S–, –Se–, –NH–, or –NRALK–, wherein RALK is a linear or branched alkyl having 1 to 10 carbon atoms or a cycloalkyl group having 3 to 10 carbon atoms;~~

~~R^3 is selected from the group consisting of:~~

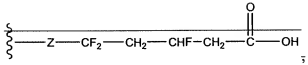


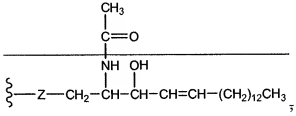
~~wherein R^5 may be the same or different and is independently a linear or branched alkyl group having from 1 to 10 carbon atoms, or a cycloalkyl group having from 3 to 10 carbon atoms;~~

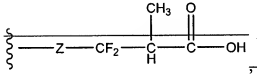
~~wherein n is an integer from 1 to 10;~~

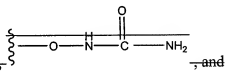
~~wherein m is 0 or 1;~~

~~wherein R^4 is a toxophore selected from the group consisting of:~~

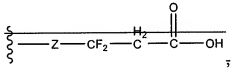








~~, and~~



wherein X is -Cl, -Br, -I, or other halogen~~, with the proviso that when R^7 is -H, and m is zero, then R^4 is not a halogen or when m is zero and n is zero, then R^4 is not a halogen;~~

~~wherein Z is independently -O- or -S-; wherein R^7 is hydrogen, a monophosphate or a phosphoramidatyl derivative of an amino acid;~~

and wherein said compound may be in any enantiomeric, diasteriomeric, or stereoisomeric form, consisting of a D-form, L-form, α-anomeric form, and β-anomeric form.

Claims 30. and 31. (Canceled).

32. (Currently Amended) The method of claim 29, wherein the compound is (E)-5-(2-bromovinyl)-2'-deoxy-5'-uridyl phenyl L-alaninylphosphoramidate~~ or (E)-5-(2-bromovinyl)-2'-deoxy-5'-uridyl phenyl monophosphate~~.

33. (Currently Amended) The method of claims 26 or 29, wherein the contacting is in vivo by administration of an effective amount of the compound to a subject in need thereof.

34. (Currently Amended) The method of claim 20, wherein the candidate therapeutic agent is contacted with the cell subsequent to contacting the cell with (E)-5-(2-bromovinyl)-2'-deoxy-5'-uridyl phenyl L-alaninylphosphoramidate ~~or (E)-5-(2-bromovinyl)-2'-deoxy-5'-uridyl phenyl monophosphate~~.

35. (Currently Amended) The method of claim 20, wherein the cell is resistant to (E)-5-(2-bromovinyl)-2'-deoxy-5'-uridyl phenyl L-alaninylphosphoramidate ~~or (E)-5-(2-bromovinyl)-2'-deoxy-5'-uridyl phenyl monophosphate~~.

36. (Canceled).

37. (New) The method of any of claims 20 or 29, wherein the cancer cell is a breast cancer cell or a colon cancer cell.